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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/591,974	09/08/2006	Keisuke Suzuki	023312-0128	4959
23428 7590 07/29/2010 FOLEY AND LARDNER LLP SUITE 500 3000 K STREET NW WASHINGTON, DC 20007				
EXAMINER				
OTTON, ALICIA L.				
ART UNIT		PAPER NUMBER		
1626				
MAIL DATE		DELIVERY MODE		
07/20/2010		PAPER		

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

### Office Action Summary

**Application No.**

10/591,974

**Applicant(s)**

SUZUKI, KEISUKE

**Examiner**

Alicia L. Otton

**Art Unit**

1626

**Period for Reply** -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 07 May 2010.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-20 is/are pending in the application.
- 4a) Of the above claim(s) 8-12 and 16-20 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-7 and 13-15 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB-08)
- Paper No(s)/Mail Date \_\_\_\_\_

- 4) ☐ Interview Summary (PTO-413)
- Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

## **DETAILED ACTION**

### ***Status of Claims***

1. Claims 1-20 are currently pending in the instant application, according to the amended Claim Listing filed May 7, 2010. Claims 8-12 and 16-20 remain withdrawn as being drawn to a non-elected invention, there being no allowable generic or linking claim.

### ***Response to Arguments and Amendments***

2. Applicant's amendments filed May 7, 2010 have been entered. All rejections and objections not explicitly maintained herein are withdrawn. The rejections below constitute the full set of rejections being applied to the instant claims.

3. The various amendments to clarify the claims overcome the objections and rejection under 35 U.S.C. 112-2<sup>nd</sup> paragraph set forth in the previously issued Office action. The rejections under 35 USC 103 and double patenting still apply for the reasons discussed in the remarks below.

### ***Maintained Claim Objections***

4. Claim 14 is objected to because in the definition of R1, the claim states that R1 may be substituted by C<sub>1</sub> to C<sub>5</sub> alkoxy, which variable is recited three times in this portion of the claim. The second and third repetitions of the phrase should be deleted.

***Response to Arguments***

5. Applicants argue with the Examiner's interpretation of the R1 definition, stating that the 2<sup>nd</sup> and 3<sup>rd</sup> recitations of C1-C5 alkoxy are meant to be a combination of two alkoxy groups [i.e. (C1 to C5)alkoxy-(C1 to C5)alkoxy]. However, the two groups are not hyphenated as in Applicant's arguments, so they would not be interpreted as being bonded to each other as part of the same group. Appropriate correction is required to clarify this definition.

***New Rejection - 35 USC § 112***

***(second paragraph)***

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claim 15 is rejected under 35 U.S.C. 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. As currently amended claim 15 is indefinite because it is drawn to a process for producing a compound of Formula I, but does not recite any active steps in the claimed process. Therefore, it is unclear what steps must be carried out in order to meet the limitations of the claim. Appropriate correction is required.

***Response to Arguments***

8. Applicants argue that claim 15 is now allowable because it was rewritten in independent form. However, this is not persuasive because the original rejection specified that in order to be allowable the claim must be rewritten in independent form to include all limitations in the base

claim (previously claim 1) and any intervening claims. The limitations from claim 1 (i.e. the process steps) were not incorporated into the new independent claim, so it is not in condition for allowance.

***Maintained Claim Rejections - 35 USC § 103***

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

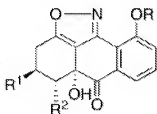
(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

10. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

11. Claims 1-7 and 13-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hachisu et al. (*J. Amer. Chem. Soc.* 2003, 125, pp.8432-8433), which has a publication date of June 21, 2003, in view of Bachman et al., *Journal of the American Chemical Society*, Vol. 57, No. 6, June 1935, pp. 1095-8.

12. Hachisu et al. teach compounds of the following formula, as well as methods of preparing the compounds utilizing a benzoin condensation mechanism:



13. The preparation methods disclosed by Suzuki et al. can be very lengthy (e.g. up to 44 hours for the reaction mechanism taught in Scheme 2). The compounds taught by Hachisu et al. differ slightly from those in the instant claims. Particularly, the instant R4 position is required to be a hydroxy group in the prior art compounds. Although R4 cannot be hydroxy in the instant claims, C1 to C10 alkoxy groups are possible. Specifically, hydrogen and methyl are deemed to be obvious variants of each other. *In re Wood*, 199 USPQ 137. Further, it has been established by the case law that the interchange of an alkyl group and hydrogen, in and of itself, is obvious. *Ex Parte Bluestone*, 135 USPQ 199.

14. Hachisu et al. do not disclose the instantly claimed production method wherein a compound of Formula (IIa) or (IIb) is treated under acidic conditions. In the claimed method, the ketone group is formed via a Pinacol rearrangement. The Pinacol rearrangement reaction is a method which is well-known in the art for being a quick and efficient method of synthesizing ketone compounds. Bachmann et al. disclose that diaryldihydrophenanthrenediols were successfully rearranged to 9,9-diaryl-phenanthrolines via treatment with a hot solution of iodine in acetic acid, without the formation of any undesired byproducts (p.1095, "Rearrangement of the Pinacols"). Although a specific temperature for the reaction is not discussed, it is disclosed that the solution is "hot" (p. 1095), and also that the reaction takes place at reflux temperature for one hour. Further, water is taught as a solvent (p.1097, "Rearrangement of the Pinacols"). There is

no evidence provided in the Bachmann reference to suggest that the reaction temperature would be outside the instantly claimed range. However, it is also noted that changing the temperature of a reaction would be considered routine optimization of a known method to a person of ordinary skill in the art and is therefore not considered inventive, absent a showing of criticality or unexpected results.

15. The motivation to make the instantly claimed compounds from the instantly claimed method derives from the expectation that structurally similar compounds would possess similar chemical activity (i.e. compounds possessing "important and potent" biological activities as disclosed by Hachisu et al.). Thus, it would have been *prima facie* obvious at the time the invention was made for one of ordinary skill in the art to produce H/alkyl analogs of the compounds taught by Hachisu et al. with a reasonable expectation of success. Motivation to develop an alternative mechanism by which to synthesize the preanthroquinone compounds of Hachisu et al. would have been provided by the Hachisu et al. reference which states that "Chemical methods for the stereocontrolled synthesis of fused-ring polyacetates currently lag far behind recent innovations in the assembly of their macrocyclic counterparts," suggesting an art-recognized problem of synthesizing the reference compounds. The motivation to specifically use the pinacol rearrangement reaction to produce the instantly claimed compounds is the fast reaction time (i.e. one hour), as disclosed by Bachmann et al., which led to an efficient ketone synthesis without the formation of any undesired byproducts. Therefore, it would have been *prima facie* obvious at the time the invention was made for a person of ordinary skill in the art to use the pinacol rearrangement method taught by Bachmann et al. to produce obvious variants of

the compounds taught by Hachisu et al. in order to obtain the claimed compounds in a faster reaction time with no formation of undesired byproduct.

*Response to Arguments*

16. Applicant's traversal is on the grounds that the instantly claimed invention is not obvious because (a) Bachman teaches pinacol rearrangement for symmetric rather than asymmetric pinacols, (b) neither reference discloses or suggests compounds of Formula I, (c) Hachisu teaches the use of a base catalyzed benzoin condensation reaction, (d) there is no apparent reason taught by either reference to combine the known elements in the fashion claimed, and (e) such a modification would have changed the principle of operation of the prior art invention.

17. Regarding traversal (a), this argument is not persuasive because Bachman teaches the conditions necessary for pinacol rearrangement in general. Although it does not explicitly exemplify an asymmetric rearrangement reaction, a person of ordinary skill in the art, when looking at the compounds of Hachisu that of the two positions having the diol groups only one is capable of having a ketone moiety attached to it due to the full valency of the other carbon. That is, the carbon to which the R<sub>4</sub> group is attached in the instant claims would not be capable of forming a ketone group being there is only one position available to form a bond. Therefore, it would be expected that the pinacolone moiety would form at the other carbon, as in the instant claims. If Applicant intends to rely on unexpected or unforeseen results, attention is invited to MPEP 716. Absent clear, convincing, side-by-side data demonstrating unobviousness vis-a-vis the prior art commensurate with the scope of protection sought, the claims are considered prima facie obvious. That is, in order to overcome this point, Applicant is invited to submit data or

evidence that the instantly claimed process would not work to produce the instantly claimed compounds utilizing the conditions for pinacol rearrangement disclosed by Bachman.

18. In response to traversal (b), applicant's argument that there is no teaching, suggestion, or motivation to combine the references, the examiner recognizes that obviousness may be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988), *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992), and *KSR International Co. v. Teleflex, Inc.*, 550 U.S. 398, 82 USPQ2d 1385 (2007). In this case, it is knowledge generally available to a person of ordinary skill in the art that hydrogen and methyl are interchangeable for one another, as described in the rejection above. *In re Wood*, 199 USPQ 137. *Ex Parte Bluestone*, 135 USPQ 199.

19. Regarding traversals (c) and (d), the Examiner recognized in paragraph 7 of the original Office action that Hachisu does not teach the treatment under acidic conditions. However, this deficiency is remedied by Bachman because Pinacol rearrangement is always carried out under acidic conditions. Hachisu does not teach the acidic conditions because Hachisu does not teach the use of Pinacol rearrangement, however given the obviousness of using Pinacol rearrangement, since it is known in the art to successfully synthesize ketone compounds, it would be obvious to also use the acidic conditions (such as acetic acid as taught by Bachman) since those are the conditions known to be necessary for such a reaction to occur. Regarding Applicant's argument that there is no apparent reason to combine the method of making the compounds of Hachisu via the Pinacol rearrangement taught by Bachman, this is not found

persuasive and was addressed in the original rejection: Motivation to develop an alternative mechanism by which to synthesize the preanthroquinone compounds of Hachisu et al. would have been provided by the Hachisu et al. reference which states that "Chemical methods for the stereocontrolled synthesis of fused-ring polyacetates currently lag far behind recent innovations in the assembly of their macrocyclic counterparts." Therefore, it was an art-recognized problem that the formation of the Hachisu compounds and other fused-ring polyacetates such as the instant compounds was not up-to-date. The synthesis in Hachisu took an very long time, as opposed to the Pinacol rearrangement in Bachman which took only 1 hour. Significantly reducing the amount of time necessary to synthesize a compound would provide the requisite motivation to try to synthesize a product by a different mechanism, when the other mechanism is known to be fast and does not form undesired by-products, as taught in Bachman. This would not result in a change in the principle of operation of the invention of Hachisu, as asserted by Applicants, because the products of Hachisu (or obvious variants thereof) would still be produced. Although the synthetic method would be different, the method was already known in the art to produce similar compounds, and represented an obvious solution to an art-recognized problem. The problems with the synthetic method were clearly addressed in Hachisu, and so changing the synthetic mechanism would have been obvious and desirable to a person of ordinary skill in the art at the time the invention was made. For at least the foregoing reasons, the instant invention is still found to be *prima facie* obvious over the combination of Hachisu and Bachman, as applied in the rejection above.

***Conclusion***

20. No claims are allowed
21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alicia L. Otton whose telephone number is (571)270-7683. The examiner can normally be reached on Monday - Thursday 8:00-6:00 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. Joseph McKane can be reached on (571)272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

22. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).
23. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

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will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

/Alicia L. Otton/  
Examiner, Art Unit 1626

/Golam M. M. Shameem/  
Primary Examiner, Art Unit 1626